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Trends in fungal colonization of pancreatic necrosis in patients undergoing necrosectomy for acute pancreatitis

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Abstract

Background. This study examines fungal colonization of post-inflammatory pancreatic necrosis in a cohort of patients undergoing open surgical necrosectomy in a single, tertiary referral unit over a 10-year period.

Methods. The charts of all patients with acute pancreatitis who underwent surgical necrosectomy during the period January 1992 to December 2001 were examined. Following exclusions a population of 30 patients were identified. There were 18 men with a median (range) age of 42 (20–69) years. Sixteen (53%) underwent surgery because of positive fine needle aspirates and the remainder underwent surgery on clinical grounds. Twenty-nine (97%) received antibiotics prior to necrosectomy. Principal outcomes were the results of microbiological culture with reference to isolation of fungi, site of isolates, trends in colonization and outcome.

Results. Candida were cultured from pancreatic necrosis in 5 (17%). These 5 individuals also had positive candidal cultures from sputum or bronchial aspirates. There were no deaths in patients with fungal colonization of necrosis. There was no change in the annual incidence of fungal colonization of necrosis over the study period.

Conclusion. Although this is a small study, there are two consistent observations: mortality in fungal colonization of necrosis was low and there was no change in the annual incidence of fungal colonization of necrosis over the decade. Discrepancies between these findings and those of previous reports mandate larger prospective evaluation.

Key Words: *Antibiotic prophylaxis, fungal infection, necrosis, necrotizing pancreatitis*

Introduction

Fungal colonization of pancreatic necrosis complicating acute pancreatitis may be a determinant of adverse outcome. Over the last decade, outcomes in favour of antibiotic prophylaxis from randomized controlled trials [1–3] and meta-analyses [4], further supported by international treatment guidelines [5,6] have resulted in the reported widespread use of broad-spectrum antibiotics [7] in the care of patients with acute pancreatitis. In turn, this has led to concerns that antibiotic-resistant organisms and, in particular, fungi may be more frequently isolated [8,9]. The present study reports on microbiological culture results in patients undergoing open surgical pancreatic necrosectomy for post-inflammatory pancreatic necrosis in a single tertiary referral hepatopancreatobiliary unit over the course of the last decade with particular reference to isolates of fungal species.

Methods

Study design

A single-centre retrospective study in patients undergoing surgery for pancreatic necrosis.

Study population

The charts of all patients with acute pancreatitis who underwent surgical necrosectomy in a tertiary referral hepatopancreaticobiliary service during the period from January 1992 to December 2001 were identified from the admissions register of the intensive care unit. Charts were reviewed and patients who underwent surgery for other complications of pancreatitis such as pseudocyst were excluded. Using current Atlanta consensus conference terminology [10], the study includes only those patients undergoing surgical débridement of infected (or suspected infected)

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pancreatic necrosis. During the period of this study, the unit policy for treatment of infected (or suspected infected) necrosis was open surgical necrosectomy involving blunt débridement without formal pancreatectomy followed by post-operative irrigation. No patients underwent minimally invasive necrosectomy. Thirty-three patients underwent open necrosectomy during this 10-year study period and fulfilled criteria for inclusion. Data from three of these patients were excluded, as microbiology results were unavailable, giving a final study population of 30. Sixteen patients (53%) underwent necrosectomy because of positive fine needle aspirates and the remainder underwent surgery on clinical suspicion of infected necrosis. Eleven (37%) underwent a single necrosectomy procedure, 5 underwent two operations and 14 (47%) underwent three operations. A deliberate decision was made to avoid attempts at allocation of antibiotic usage into prophylactic or treatment categories as data were analysed retrospectively and the indication for antibiotic use was not consistently documented.

Demographic data

There were 18 men with a median (range) age of 42 (20–69) years. The aetiology of acute pancreatitis was alcohol in 16 (53%), gallstone in 10 (33%) and other causes in 4. The median (range) APACHE II on admission was 9 (1–18).

Microbiological evaluation

Microbiological culture results from the following specimens were evaluated: fine needle aspiration of pancreatic tissue; pancreatic abscess material or infected necrosis retrieved at surgery; peripheral and line withdrawal blood cultures; and samples from other sites such as bronchial secretions, urine, intravenous catheters and peritoneal fluid. All specimens/swabs were examined microbiologically for aerobic and anaerobic bacteria and fungi. For cultivation of fungi, swabs were streaked on Sabouraud dextrose agar (Oxoid, Basingstoke, UK) incubated aerobically at 30°C for 48 hours. Yeast-like colonies growing on primary isolation media were routinely Gram stained. Yeasts discovered on microscopy were identified to the species level by the ability to form germ tubes and by the API ID 32C test (bioMérieux UK Limited, Basingstoke, England).

Principal outcomes

Results are analysed in the following categories:

Microbiological isolates: the results of microbiological cultures with particular reference to isolation of fungi and site of fungal isolates.

Trends in fungal colonization of necrosis over the study period: data were grouped into 5 periods (1992/93, 1994/95, 1996/97, 1998/99 and 2000/01).

Statistical analyses

Data are presented as median (range). As this study presents observational data in small groups, inter-group statistical comparisons would be inappropriate.

Results

Microbiological isolates

Figure 1 shows the results of all positive cultures in the 30 patients. Fourteen patients had bacterial colonization alone (without fungal colonization). A further five had positive fungal isolates in addition to bacteria. Eleven patients (37%) had sterile necrosis. All fungal species isolated in this study were *Candida albicans spp*. These five individuals also had positive candidal cultures from sputum or bronchial aspirates isolated during the post-necrosectomy period. In addition to pancreatic necrosis and sputum, one of these patients had a further positive culture from a central line and another patient had a positive culture for candida from an abdominal wound.

Overall, 29 (97%) received antibiotics prior to necrosectomy with the most frequently prescribed being a second-generation cephalosporin in 17 (57%). The median duration of antibiotic use was 29 (4–54) days. Antifungal therapy was used in 14 patients (fluconazole in 11 and amphotericin in 3). All five patients with positive candidal isolates had received pre-operative antibiotics and two (40%) had received anti-fungal therapy (1 fluconazole and 1 amphotericin). In the 19 patients with infected necrosis there were 30 positive bacterial isolates (see Figure 1) as 7 patients had polymicrobial contamination of necrosis.

Trends in fungal colonization over the study period

Annual isolates of fungi are seen in Table I. Expressed as a proportion of patients undergoing necrosectomy,

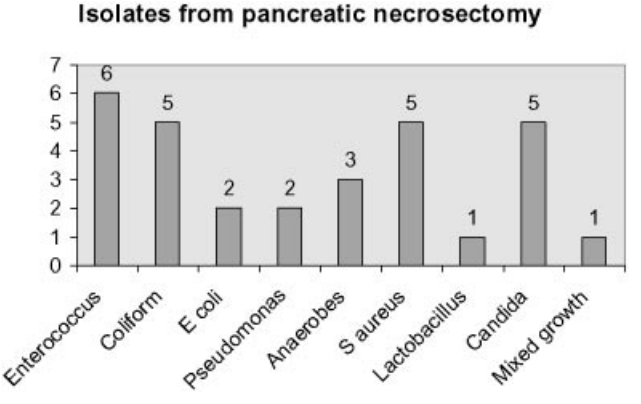

Figure 1. Microbiological isolates from pancreatic necrosectomy. The total numbers of positive microbiological cultures from all sites in the 30 patients. Note that all five patients with *candida* had positive isolates from pancreatic necrosis. Numbers on the y-axis refer to actual numbers. Seven patients had polymicrobial colonization of necrosis.

Table I. Trends in fungal colonization of pancreatic necrosis complicating acute pancreatitis over 10 years

	Trends in fungal colonization				
Years	1992–93	1994–95	1996–97	1998–99	2000–01
Number of patients	6	2	5	8	9
Antibiotic use prior to surgery	5 (83)	2 (100)	5 (100)	8 (100)	9 (100)
Sterile necrosis	3	0	3	3	2
Necrosis (bacteria only)	2	2	1	4	5
Necrosis (fungi+/−bacteria)	1 (17)	0	1 (20)	1 (13)	2 (22)

Data are grouped in two-year periods. Numbers in parentheses are percentages of patients undergoing necrosectomy during each two-year period.

Table II. Fungal colonization of post-inflammatory pancreatic necrosis – present results compared to three recent reports

			Fungal colonization of pancreatic necrosis		
First author and year of publication	Study period	Number of patients with infected necrosis	Number of patients	Number of deaths	Mortality rate
Isenmann R, 2002 [12]	1982–1997	92	22 (24%)	14 (64%)	64%
Gloor B, 2001 [8]	1994–2000	33	8 (24%)	2 (25%)	25%
Hoerauf A, 1998 [9]	1987–1993	37	13 (35%)	7 (54%)	54%
Present study	1991–2001	30	5 (17%)	0	0

fungal colonization of necrosis ranges from 0% to 22% over the study period. Overall there were seven deaths, giving a mortality rate of 23%. Four deaths occurred in patients with sterile necrosis and three in patients with infected necrosis. There were no deaths in patients with fungal colonization of necrosis.

Discussion

The present study has applied current nomenclature to a population of patients undergoing necrosectomy for pancreatic necrosis complicating acute pancreatitis, in a single tertiary referral unit over a 10-year study period. The advantages of a well-defined study cohort are to an extent offset by the small patient numbers in the resulting population. The sample size could have been augmented most simply by including all patients undergoing intervention/abdominal aspiration for acute pancreatitis. However, in a retrospective analysis if patients undergoing percutaneous aspiration outwith the intensive care environment are considered, disease descriptors are less reliable (for example, the distinction between post-inflammatory fluid collection, acute pseudocyst and pancreatic abscess) and thus any gain in sample size would have been offset by increased heterogeneity within the data. Thus a pragmatic decision was made to accept the reality of a small but well-defined patient population and accordingly descriptive data are presented.

An interesting finding is that although fungal colonization was present in five (17%) of patients undergoing necrosectomy in this series there were no deaths in this group. Although this finding is from a small cohort and therefore of limited weight it is nonetheless valid as observation. Further, these data are important as they are in contrast to a previous report from the senior author based on patients undergoing pancreatic necrosectomy in the Edinburgh HPB unit where fungal colonization of necrosis was associated with an 80% mortality [11]. One possible explanation for the difference is that larger studies are required to carefully document the incidence and influence of fungal colonization in patients with pancreatic necrosis. The annual colonization rates are, however, in keeping with results from three recent studies over similar recruitment periods (Table II). Equally, the findings of this study are counter to the viewpoint that candidal colonization of necrosis is a predictor of adverse outcome [12] and also (although again the numbers are small) this study revealed no evidence of a major change in fungal colonization rates over the 10 years spanned by the study.

In conclusion, this small cohort study reviews data from patients undergoing open surgical necrosectomy for post-inflammatory pancreatic necrosis over a decade. The low mortality in patients with fungal colonization of necrosis is an important finding in that it suggests that, at the least, further adequately powered studies are mandated to accurately quantify the incidence and risk of fungal colonization and to detect any association with the widespread use of antibiotic prophylaxis.

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